REMARKS

Status of Claims

Claims 19-60 are pending. New claim 61 is added. No new matter is entered by this amendment.

Claim Rejections: 35 U.S.C. § 103(a)

Claims 19-60 were rejected under 35 U.S.C. § 103(a) for reciting subject matter unpatentable over U.S. Pat. No. 4,625,725 to Davison et al.

These claims specify a surgical tool having a cutting surface that has fewer than about 10 pores per square centimeter that are greater than about 15 nanometers, 12 nanometers, 10 nanometers, or 5 nanometers in size (depending on the claim). Various claims further specify other properties of the tool, such as material of composition, density, and tool structure; additional claims specify methods of making the tools.

While acknowledging that the cited art does not teach any of the claimed properties, the Examiner stated that it would have been obvious to select them.

Applicants ask the Examiner to reconsider and withdraw the rejection because it would not have been obvious to form a surgical tool cutting surface with so low a porosity as that claimed. There was no recognized need or application for such a low porosity surface at the time Applicants made the invention. Thus the selection of the claimed porosity would have been an arbitrary one before Applicants' invention, unsupported by any reason or rationale in the prior art. The claimed subject matter is therefore nonobvious.

As discussed in the patent application, Applicants realized that providing a reusable surgical instrument with a cutting surface having the low porosity claimed would reduce or eliminate the transmission of prion proteins from one patient to the next *yet still allow sterilization using conventional techniques*.

Prion proteins are the well-known cause of diseases such as bovine spongiform encephalopathy ("mad cow disease") and the related human Creutzfeldt-Jakob disease ("CJD"). CJD has been clinically proven to be transmissible from one patient to the next by use of contaminated surgical instruments. At the time of the invention, such "iatrogenic" (i.e., caused by the medical treatment itself) transmission of CJD and other prion diseases by

re-using surgical instruments was recognized as so serious a problem that the UK National Health Service in 2001 ordered that all tonsillectomies must be performed using single-use surgical instruments (Frosh, "Iatrogenic vCJD from surgical instruments," *Brit. Med. J.*, 322:1558-1559, 2001).[1] Around the same time, the World Health Organization issued stringent guidelines for the cleaning and sterilization of re-usable instruments to prevent prion transmission (WHO Guidelines 2000, section 6.2 and Annex III).[2] Among other steps, the guidelines call for immersion in highly concentrated sodium hydroxide (a 1 molar solution), a treatment which few surgical-grade materials can long withstand. Health authorities called for these extreme measures because prions had proved remarkably resistant to conventional sterilization techniques, such as detergent, scrubbing, protease digestion, heat, radiation, and formaldehyde.[3]

But a problem remained even with these guidelines because their implementation was prohibitively expensive: either use a new instrument for each procedure (the UK guidelines), or subject the instrument to a sterilization protocol that would destroy it after only a few uses (the WHO guidelines).

The assumption underlying these approaches to the prion transmission problem was that it would be solved by some manipulation of the instrument: i.e., by discarding it after every use or sterilizing it under brutal conditions. There was no suggestion in the art that changes to the material properties of the cutting edge itself would provide a solution. Thus, even to pose the question "what can we do to the cutting surface to make standard sterilization effective against prions?" was to do something that was not obvious at the time the invention was made.

Yet that is exactly what Applicants did. They conceived that a better solution to the problem of making a surgical instrument safe for reuse where prion proteins were of concern was to *alter the material properties of the cutting surface so that it could be safely sterilized in a conventional manner*, rather than change how the instrument was processed (i.e.,

[1] Copy attached as Exhibit A.
[2] Cited sections attached as Exhibit B.
[3] In the United States, the FDA and CDC were studying the problem of iatrogenic CJD but had not issued their own guidelines at the time of the invention.

throwing it away each time or subjecting it to damagingly stringent sterilization).

In particular, Applicants noticed that prion proteins are so small (35 to 50 angstroms in size = about 1-2 ten-millionths of an inch) that they could easily fit inside the pores normally present on a cutting surface, even though the surface appears smooth and nonporous to the human eye. The prions would thereby be sheltered from routine sterilization techniques, such as scrubbing the cutting edge to remove organic matter or exposing the surface to chemicals; the scrub bristles and chemicals simply cannot penetrate pores that can accommodate prions, because the pores are so small. By comparison, bacteria (about 10,000 angstroms = 1 micron) and viruses (200 angstroms and larger) are far larger than prions and considerably more easily cleaned from the porous surface of stainless steel.

So Applicants realized that they could prevent prion adhesion by eliminating (or substantially eliminating) pores in the cutting blade large enough to harbor a prion. The prions would thereby no longer be sheltered and could be cleaned off the surface with conventional sterilization techniques. Applicants would thus eliminate the need to resort to single-use blades or destructive sterilization. They concluded that reducing the surface porosity to fewer than about 10 pores per square centimeter that are greater than about 15 nanometers (= 150 angstroms) in size would substantially reduce prion loading (i.e., reduce the amount of prion protein remaining on the blade to below that of an infective dose). Applicants concluded that even lower levels of porosity would be useful and were achievable as well.

Such a low level of porosity had never been previously considered necessary or even desirable for use on surgical instrument cutting tools (to Applicants' knowledge and in the art of record) because it would have served no purpose known at the time on invention. While one could conjecture that practitioners might have sought cutting surfaces with sufficiently low porosity to exclude bacteria and viruses (though there is no evidence of this in the art of record), such porosity would be insufficient to exclude prions. Only once Applicants realized that the high porosity of existing surgical instruments was the root cause of prion resistance to sterilization did the solution become apparent: reduce the porosity.

Stainless steel cannot possibly achieve the claimed low porosity because its density (7–8 g/cm^3) is far too low; and while varieties of nickel carbide in existence before the filing

of the patent application have adequate densities, they still do not achieve the claimed surface porosity unless processed in the various ways disclosed by Applicants (such as polishing with diamond polishing compound, or forming the surface with fine grade carbide particles, or subjecting to hot isostatic pressing). And although the techniques to achieve the low porosity might have been known in the art, no one had thought of applying them in the manner Applicants disclose to achieve the claimed products and methods

No reference in the record discloses achieving such low porosity, and for good reason: until prions were generally accepted in the 1990's as infectious particles, there was no reason to make surgical instruments with porosity low enough to exclude them. And once prions were so identified, health authorities around the world urged destruction or harsh sterilization of surgical instruments to prevent prion spread.

Applicants' approach represented an entirely distinct way of looking at the problem. Their solution contributed significantly to the art by providing surgical instruments that can be cleaned using conventional techniques and yet be safe to use for situations in which prion transmission is a concern. Applicant's carefully-selected porosity parameters for cutting surfaces are no mere design choice as dismissed by the Examiner, nor did they result from the exercise of routine skill. Rather, they resulted from Applicants' insight into, and careful consideration of, the mechanism of prion transmission, an approach which had eluded all prior comers.

The claimed subject matter is therefore not obvious, and Applicants ask the Examiner to withdraw the rejection.

Respectfully submitted,

Date: September 25, 2008
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